

Remarks

In the outstanding Official Action, the Examiner:

(1) rejected claims 1, 3-4, 11-12 and 19 under 35 USC 102(b) as being anticipated by Paradies (U.S. Patent No. 4,870,174) ("Paradies");

(2) rejected claims 1, 3-4, 11-15 and 19 under 35 USC 102(b) as being anticipated by Short et al. (U.S. Patent No. 5,578,119) ("Short");

(3) rejected claims 1, 3-4, 7 and 19 under 35 USC 102(e) as being anticipated by Eini et al. (U.S. Patent Application Publication No. 2004/0253275) ("Eini");

(4) rejected claims 1, 3-4, 6, 13 and 19 under 35 USC 102(b) as being anticipated by Chen et al. (U.S. Patent Application Publication No. 2003/0157178) ("Chen");

(5) rejected claims 1, 3-5, 11, 13-15 and 19 under 35 USC 102(b) as being anticipated by Luissi et al. (U.S. Patent No. 4,587,284) ("Luissi");

(6) rejected claims 1, 3-4, 6, 13-15 and 19 under 35 USC 102(b) as being anticipated by Marchant et al. (U.S. Patent No. 6,297,337) ("Marchant");

(7) rejected claims 1, 3-5, 11-15 and 19 under 35 USC 102(b) as being anticipated by Wokalek et al. (U.S. Patent No. 4,905,700) ("Wokalek");

(8) rejected claims 1, 3, 7, 11-15 and 19 under 35 USC 102(e) as being anticipated by Young et al. (U.S. Patent Publication No. 2003/0180347) ("Young"); and

(9) rejected claims 1, 3-5 and 19 under 35 USC 102(b) as being anticipated by Pfirrmann et al. (International Publication No. WO 94/03174) ("Pfirrmann").

With respect to Items 1-9 above, Applicant has now amended claim 1 so as to further define the present invention. Support for this amendment can be found at page 15, line 28 - page 16, line 2 and at page 16, line 5 - page 16, line 6. On account of the foregoing change and the following remarks, Applicant respectfully submits that this application is in condition for allowance and respectfully requests reconsideration.

The claims currently under active prosecution in this case consist of claims 1, 3-7, 11-15 and 19. Claim 1 is independent, and claims 3-7, 11-15 and 19 all depend, either directly or indirectly, from claim 1. Therefore, the limitations of claim 1 are present in all of the claims currently under active prosecution in this case.

Claim 1 currently reads as follows:

1. *A composition comprising:*

a thixotropic gel; and

an antimicrobial agent contained in the thixotropic gel;

wherein the thixotropic gel is characterized by:

(i) free flow upon the application of a threshold level force imparted by a conventional medical syringe such that the composition may be instilled into a hemodialysis catheter using such a conventional medical syringe so as to completely fill the hemodialysis catheter, and easily withdrawn from the hemodialysis catheter using such a conventional medical syringe;

(ii) sufficient cohesiveness such that, when the composition is moved through the lumen of a hemodialysis catheter using a conventional medical syringe, the composition advances through the lumen as a cohesive rod-shaped mass; and

(iii) when the composition is disposed within the lumen of a hemodialysis catheter which is installed in the vascular system of a patient, the composition remains in the lumen; and wherein the thixotropic gel is biocompatible and biodegradable in blood.

Thus, claim 1 calls for a composition which comprises a thixotropic gel and an antimicrobial agent contained in the

thixotropic gel, wherein the thixotropic gel is characterized by five specific attributes:

(i) free flow upon the application of a threshold level force imparted by a conventional medical syringe such that the composition may be instilled into a hemodialysis catheter using such a conventional medical syringe so as to completely fill the hemodialysis catheter, and easily withdrawn from the hemodialysis catheter using such a conventional medical syringe (sometimes hereinafter referred to as the "syringability" attribute);

(ii) sufficient cohesiveness such that, when the composition is moved through the lumen of a hemodialysis catheter using a conventional medical syringe, the composition advances through the lumen as a cohesive rod-shaped mass (sometimes hereinafter referred to as the "plug flow" attribute);

(iii) when the composition is disposed within the lumen of a hemodialysis catheter which is installed in the vascular system of a patient, the composition remains in the lumen (sometimes hereinafter referred to as the "lock integrity" attribute);

(iv) it is biocompatible (sometimes hereinafter referred to as the "biocompatibility" attribute; and

(v) it is biodegradable in blood (sometimes hereinafter referred to as the "biodegradability" attribute).

None of the nine references cited by the Examiner contains all of the foregoing limitations - which is to be expected, since these limitations are specifically chosen so as to enable the composition to be used as a catheter lock, and none of the references were designed for a similar application.

Specifically, Paradies teaches specific types of compounds which can be used as pharmaceuticals. Paradies does not disclose the rheological properties of his compounds, except that in Example 9, Paradies mentions a way to produce an emulsion which has thixotropic properties. However, Paradies does not disclose exactly what characteristics are embodied in the gel, or what the specific property values are for those characteristics. Among other things, Paradies does not teach a thixotropic gel which flows freely under the forces imparted by a conventional medical syringe, moves through a catheter as a cohesive rod-shaped mass, and remains in the lumen of a catheter when installed in the vascular system of a patient. Thus, Paradies does not teach a thixotropic gel having the "syringability", "plug flow" and "lock integrity" attributes discussed above. Furthermore, Paradies does not teach that the gel is biodegradable in blood, i.e.,

Paradies does not teach the "biodegradability" attribute discussed above. For these reasons, Paradies is not believed to disclose or render obvious the present invention.

Short describes the material properties of a sculpting medium (i.e., something like clay). Short notes that the material can be formed so that it does not exhibit elastic memory (see column 7, line 20). This means that the Short material does not exhibit "die swell" characteristics, which is essential if the material is to pass through the narrow tip of a syringe and then expand or spring back so as to fill the catheter. This is important, since the catheter lock must contact the side walls, thereby enabling "lock integrity". Thus, Short does not teach a thixotropic gel having the "syringability" attribute discussed above. Furthermore, it is not clear that Short discloses the "lock integrity" attribute discussed above. Finally, Applicant questions whether Short teaches a material which has the "biocompatibility" and "biodegradability" attributes discussed above. For these reasons, Short is not believed to disclose or render obvious the present invention.

Eini teaches a viscoelastic material which is semi-solid at rest but exhibits liquid properties upon application of shear forces. However, Eini does not disclose any other rheology

properties or values for his material. Eini does not disclose that the material can be used with a syringe to withdraw the gel from a location. Also, Eini makes no mention of die swell which, as discussed above, is essential if the gel is to pass through the narrow tip of a syringe and then expand to fill a catheter and thereby enable "lock integrity". Thus, there is no reason to believe that Eini teaches a thixotropic gel which has the "syringability", "plug flow" or "lock integrity" attributes discussed above. Furthermore, Eini mentions at [0062] - [0065] that fatty substances are preferred embodiments, which may not allow dissolution in the bloodstream. Thus, there is also no reason to believe that Eini teaches a material which has the "biodegradability" attribute discussed above. For these reasons, Eini is not believed to disclose or render obvious the present invention.

Chen describes methods and properties to make specific biocompatible thixotropic gels which can be drug carriers and injected with a syringe into patients. Chen further discloses the characteristics needed to enable one to inject the gel into subjects. However, Chen makes no mention of many critical aspects of the present invention, such as the die swell, plug flow and yield strength needed for the "syringability", "plug

flow" and "lock integrity" attributes discussed above. More particularly, Chen describes viscosity ranges suitable for injection from a special Hamilton Syringe (i.e., a long, thin laboratory syringe having a construction different from a conventional medical syringe and producing pressures three to four times that obtained with a conventional medical syringe) into a short needle. Chen makes no mention of withdrawing the gel back into the syringe, and certainly not in the context of withdrawing the gel back through a long catheter of the sort used in hemodialysis applications. Although the viscosity values described by Chen are acceptable for injection, they are not acceptable for the suction withdrawal of the gel. In this respect it should be appreciated that, during injection with a conventional medical syringe, one can produce pressure levels of 3 to 4 atmospheres (i.e., up to approximately 3000 mm Hg pressure). However, a syringe in "sucking" mode can theoretically produce a pure vacuum which only allows a driving pressure of 1 atmosphere (i.e., 760 mmHg). In reality, the driving pressure of a "sucking syringe" is much lower than a pure vacuum, primarily because air and water vapor and other gases dissolved in the gel come out of solution and, as these gases stay in the expanded space of the syringe during suction, do not

allow one to reach a perfect vacuum. Applicant has run experiments showing that gels being sucked into a small syringe usually have pressures which produce a suction pressure difference of approximately 500 mm Hg or even less. This is, then, the worst case condition regarding the ability to move a gel with a "sucking" syringe in order to overcome the yield strength and start gel movement and enable reductions in viscous drag (thixotropic characteristic) so as to enable easy gel movement. For these reasons, it is believed that Chen does not disclose a material having the "syringability", "plug flow" and "lock integrity" attributes discussed above. Furthermore, Figs. 5, 6A and 6B of Chen suggest that the dissolution rate of the Chen gels is much too slow for Applicant's gel requirements, as it must dissolve in a matter of hours at most (rather than weeks). Thus, Chen also does not disclose a material having the "biodegradability" attributes discussed above. For these reasons, Chen is not believed to disclose or render obvious the present invention.

Luissi describes a gel drug carrier, but does not describe specific rheology properties for the gel. In fact, the Luissi gel is not even thixotropic. Only the property of a gel drug carrier is described. Thus, Luissi does not disclose a material

having the "syringability", "plug flow" and "lock integrity" attributes discussed above. For these reasons, Luissi is not believed to disclose or render obvious the present invention.

Marchant teaches how to formulate a polymer so as to provide selected rheological properties (e.g., a particular yield stress value, or a Brookfield viscosity value, or a microviscosity value, etc.). However, this is not the same as teaching Applicant's claimed composition. Applicant's claimed composition simultaneously provides five different attributes, i.e., the aforementioned "syringability", "plug flow", "lock integrity", "biocompatibility" and "biodegradability" attributes. Nowhere does Marchant teach a specific formulation so as to simultaneously provide all five of these attributes, nor does Marchant provide any motivation for doing so, inasmuch as Marchant is concerned with providing a new polymer formulation for use as bioadhesive, thickener, emulsifier, suspending aids and pharmaceutically controlled release excipients, rather than providing a catheter lock. For these reasons, Marchant is not believed to disclose or render obvious the present invention.

Wokalek does not teach a thixotropic gel, much less a thixotropic gel having the aforementioned "syringability", "plug flow", "lock integrity", "biocompatibility" and

"biodegradability" attributes. Wokalek is not believed to provide any description of rheological properties - the Wokalek composition appears to be a soft, solid-like sheet of material, intended primarily to facilitate ultrasound transmission, and does not appear to be flowable. For these reasons, Wokalek is not believed to disclose or render obvious the present invention.

Young discloses an adhesive bandage-like pad comprising a hydrogel matrix to deliver drug through the skin. Young is silent with respect to specific rheological properties of the sort which are critical to the present invention, i.e., the aforementioned "syringability", "plug flow" and "lock integrity" attributes. Furthermore, Young is not believed to teach the "biodegradability" attribute of the present invention. For these reasons, Young is not believed to disclose or render obvious the present invention.

Pfirrmann discloses methods for using taurolidine compositions for dental applications. Pfirrmann notes that the composition may be a gel which can be injected with a syringe (see page 8, 2nd complete paragraph). However, no mention is made regarding gel yield strength, or a viscosity low enough to allow suction with a syringe, or die swell, or plug flow, etc. One hydroxycellulose gel is described on the bottom of page 9 to

the top of page 10, but there is no description of specific properties which would enable use as a catheter lock. Applicant notes that a commercial hydroxycellulose taurolidine gel made by TauroPharm for dental use has no yield strength, and hence no "lock integrity". Thus, Pfirrmann does not appear to teach the aforementioned "syringability", "plug flow" and "lock integrity" attributes of the present invention. For these reasons, Pfirrmann is not believed to disclose or render obvious the present invention.

On account of the foregoing, Applicant submits that claims 1, 3-7 and 11-15 and 19 are in condition for allowance. Early and favorable reconsideration is therefore respectfully requested.

Thank you.

Respectfully submitted,



Mark J. Pandiscio

Registration No. 30,883

Pandiscio & Pandiscio, P.C.

470 Totten Pond Road

Waltham, MA 02451

Tel. (781) 290-0060